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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/964,899	09/27/2001	Dalia Cohen	4-31612A/USN	3252
1095	7590	07/28/2004	EXAMINER	
NOVARTIS CORPORATE INTELLECTUAL PROPERTY ONE HEALTH PLAZA 430/2 EAST HANOVER, NJ 07936-1080			BERTOGGIO, VALARIE E	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/964,899

Applicant(s)

COHEN ET AL.

Examiner

Valarie Bertoglio

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**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-111 is/are pending in the application.
- 4a) Of the above claim(s) 4-26 and 31-109 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 27-30, 110 and 111 is/are rejected.
- 7) ☐ Claim(s) 1, 27 and 111 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on N/A is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's amendment filed 05/28/2004 has been entered. Claims 1 and 27 have been amended. Claims 110 and 111 have been added. Claims 4-26 and 31-109 are withdrawn as being drawn to a non-elected invention. Claims 1-111 are pending and claims 1-3, 27-30, 110 and 111 are currently under consideration.

### ***Election/Restrictions***

This application contains claims 4-26 and 31-109, drawn to an invention nonelected with traverse in the reply filed on 11/26/2003. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### ***Claim Objections***

The objection of claims 1 and 27 is maintained because of the following informalities:

Claims 1 and 27 have grammatical issues. As set forth in the previous office action mailed 01/29/2004, the phrase "and expressing said DNA sequence" in claim 1 and claim 27, step (a), does not fit with the rest of the claim. Appropriate correction is required.

Claims 111 is objected to because of the following informalities:

Claim 111 does not end with the proper punctuation.

Applicant failed to respond to the objection.

### ***Allowable Subject Matter***

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Claim 3 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-3 and 27-30 under 35 U.S.C. 112, first paragraph is maintained and applied to newly added claims 110 and 111, because the specification, while being enabling for a transgenic fly comprising a DNA sequence encoding Abeta42 operably linked to an eye-specific expression control sequence wherein expression of said DNA sequence results in said fly displaying a rough eye phenotype and a method of using said fly to identify compounds that treat or ameliorate neural degeneration, does not reasonably provide enablement for said fly wherein the DNA sequence encoding Abeta42 is operably linked to any tissue-specific expression control sequence wherein expression of said DNA sequence results in said fly displaying any phenotype in a neural tissue or a method of using said fly. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The breadth of the claims encompasses a transgenic fly comprising an Abeta42 transgene operably linked to any tissue specific expression control sequence wherein expression of the transgene results in any altered phenotype in any neural tissue. Furthermore, the claims

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encompass any tissue-specific expression wherein an altered phenotype results anywhere in any tissue, including those tissues not expressing the transgene, and not necessarily in the neural cells of that tissue.

Applicant has argued that the state of the art of transgenics in 2001 was that techniques in the transgenic field were routine and conventional (page 18, last paragraph). Applicant points out a plethora of sources of characterized fly lines and promoters that are known to drive gene expression in specific spatial and temporal patterns. With this as support, Applicant contends that the unpredictability of phenotype in transgenics is unfounded. Applicant has also amended claims to limit the scope of the phenotype claimed to encompass any altered phenotype in a tissue comprising neuronal cells.

In response, the rejection set forth on pages 3-7 of the previous office action is not drawn to whether the skilled artisan could generate a transgenic fly overexpressing Abeta42 in any particular tissue or that said fly would likely exhibit a phenotype. The rejection is based on the unpredictability of what the resulting phenotype would actually be when other control elements that are not specific to the eye are used. As set forth by the instant specification, the same construct leads to variable levels of expression of Abeta42, which results in variations in the severity of the rough eye phenotype resulting from Abeta42 overexpression. Low levels of expression in some lines caused phenotypes that were not detectable macroscopically (page 49, line 25-page 50, line 2). In fact, some flies did not exhibit a rough eye phenotype at all (page 46, lines 24-25). Based on the unpredictability of phenotype in transgenics as set forth above and in the previous office action, one of skill in the art cannot predict what phenotype will result in any neuronal cell containing tissue when any expression control sequences are used. Claims 110

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and 111 limit the fly, comprising a transgene with any tissue specific promoter, to displaying an altered phenotype in a tissue selected from the group consisting of eye, wing, notum, brain, CNS and PNS. An eye specific promoter is unlikely to have any effect on the phenotype of a wing. Such a scenario is encompassed by the claims and supported by the instant specification.

Furthermore, it cannot be predicted what phenotype would result from expression of Abeta42 in any tissue other than the eye. For example, if Abeta42 were expressed in the wing, anywhere in the wing as encompassed by the claims, would the fly exhibit wing degeneration, small wings, large wings, curly wings, or neural degeneration in an otherwise normal wing, or some other phenotype? The specification is only enabling for a transgenic fly comprising a DNA sequence encoding Abeta42 operably linked to an eye-specific control sequence wherein expression of the DNA sequence causes a rough eye phenotype. The above rejection as it applies to claims to the fly, also applies to claims drawn to methods of using the fly encompassed by claims 27-30. One of skill in the art would not know how to use the fly broadly encompassed by the claims without undue experimentation to determine the phenotype and to determine how to use the fly with the newly determined phenotype. One of skill in the art would not know what to screen for or how to use a compound identified in the method. If the altered phenotype is small wings, would a compound that caused larger wings necessarily treat neural degeneration?

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claim 111 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 111 is unclear because it refers to the transgenic fly of claim 30; however, claim 30 is a method claim.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Valarie Bertoglio  
Examiner  
Art Unit 1632

DEBORAH CROUCH  
PRIMARY EXAMINER  
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